Title
POTENTIAL RISKS FROM EXPOSURE TO ORGANIC CARCINOGENS IN INDOOR AIR

Authors
McCann, J.
Horn, L.
Girman, J.

Publication Date
1986-10-01

Lawrence Berkeley Laboratory
UNIVERSITY OF CALIFORNIA

APPLIED SCIENCE DIVISION

Presented at the EPA Symposium on the Application of Short-term Bioassays in the Analysis of Complex Environmental Mixtures, Durham, NC, October 20–23, 1986, and to be published in the Proceedings

Potential Risks from Exposure to Organic Carcinogens in Indoor Air

J. McCann, L. Horn, J. Girman, and A.V. Nero

October 1986

APPLIED SCIENCE DIVISION

Prepared for the U.S. Department of Energy under Contract Number DE-AC03-76SF00098.

DISCLAIMER

Presented at the EPA Symposium on the
Application of Short-term Bioassays in
the Analysis of Complex Environmental
Mixtures. Durham, NC. October 20-23, 1986.
To Appear in the Proceedings of the Conference.

LBL-22474

POTENTIAL RISKS FROM EXPOSURE TO ORGANIC CARCINOGENS IN INDOOR AIR

Joyce McCann, Laura Horn, John Girman*, and A.V. Nero

Indoor Environment Program
Applied Science Division
Lawrence Berkeley Laboratory
1 Cyclotron Road
Berkeley, CA 94720

*Air and Industrial Hygiene Laboratory
California Department of Health Services
Berkeley, CA 94704

October 1986

This work was supported by the Director, Office of Energy Research Office of Health and Environmental Research, Human Health and Assessments Division of the U.S. Department of Energy under Contract No. DE-AC03-76SF00098.

Presented at EPA Symposium on the
Application of Short-term Bioassays in
the Analysis of Complex Environmental
Mixtures. Durham, NC. October 20-23, 1986.
To Appear in the Proceedings of the Conference.

POTENTIAL RISKS FROM EXPOSURE TO ORGANIC CARCINOGENS IN INDOOR AIR

Joyce McCann, Laura Horn, John Girman*, and A.V. Nero

Indoor Environment Program
Lawrence Berkeley Laboratory
Berkeley, CA

Current Address:
Indoor Air Quality Program
Air and Industrial Hygiene Laboratory
California Department of Health Services
Berkeley, CA 94704

INTRODUCTION

Increasing experience with "complaint, "sick", or "tight" buildings suggests the occurrence of adverse effects on humans from exposure to organics in indoor air. However, but for a few exceptions such as formaldehyde, chlordane, and pentachlorophenol, the complaints cannot be attributed with any certainty to individual chemicals. Furthermore, while the experience to date constitutes an important indicator of a potential problem, complaints are generally limited to acute or irritant effects, such as unpleasant odors, respiratory or eye irritation, or headaches. Thus complaints rarely serve as effective indicators of more life-threatening end points, such as cancer or reproductive effects, if only because individuals are not likely to be able to associate such toxic effects with the air inside the buildings they occupy.

These limitations on our experience with complaint buildings have so far precluded either 1) an assessment of the overall importance of organics indoors as a cause of any class of toxic effects, or 2) identification of the most important contributors to such effects. Nonetheless, substantial data are available, primarily from other types of studies, on the toxic effects of many of the chemicals that occur indoors. Effective utilization of information from animal and human toxicology can help narrow

the focus of future studies by targeting high-risk chemicals and help identify toxic effects to be examined in epidemiological studies.

We have examined the current literature reporting concentrations of organics in indoor environments to construct a nominal list of indoor air concentrations for 140 compounds. We have gone on to examine, in a preliminary way, the potential risk of various health endpoints from indoor air exposure to these substances (McCann, et al., 1986). An important component of this study has been to examine risks for the carcinogens among these substances. We here report our preliminary assessment of cancer risks from exposure to 24 carcinogens, using several analytical approaches.

METHODS

Assembly of a nominal list of indoor air concentrations of organic carcinogens.

The primary sources for the full list of compounds examined in this study were the published literature and presentations made at the 1984 Indoor Air Quality meetings in Sweden. We have not tried to survey the literature exhaustively, but rather to assemble a representative collection of information on which we could base a preliminary analysis.

Table 1 lists indoor air concentrations for 24 carcinogens among the full set of chemicals examined. From each study we have, when possible, recorded the maximum and the median (or mean) values measured. All concentration data are direct field measurements in homes and public buildings. Our main focus was to assemble concentration measurements that reflected everyday exposure in normal (non-complaint) homes and offices. Thus, we have not included, for example, concentrations of formaldehyde in UFFI homes or high concentrations of benzo[a]pyrene from bituminous coal used in cooking stoves in small dwellings in India (Dave, 1984). Also not included are concentrations measured in traditional occupational settings.

Calculation of carcinogenic risk.

Scaling factors. The principal basis for our estimates of cancer risk are the data from animal studies and TD50s estimated by Gold, et al (1984,1986). The TD50 is the daily dose, administered over a lifetime that will result, on the average, in one-half of the test population remaining tumor free. Conversion from an oral dose in rodents to its approximate inhalation equivalent in humans (we have called this the 'human-equivalent TD50') was as follows (Anderson, et al., 1983): We assumed 100%

absorption via both oral and inhalation routes, and we also assumed that different breathing rates of humans and rodents result in roughly the same daily intake per unit body weight from inhalation of chemicals present at the same airborne concentrations. Thus, to obtain the human-equivalent airborne concentration, the average daily oral dose (in mg/kg/day) was divided by the breathing rate of the test animal (rat: 0.64 m^3/kg/day; mouse: 1.3 m3/kg/day) (Anderson, 1983). In the three cases where chemicals were administered via the inhalation route (1,2-dibromoethane, formaldehyde, and vinylidene chloride) we used the same scaling factors as Gold, et al. to estimate the 24-hour airborne exposure in ug/m^3. For dichloromethane, the only carcinogen we examined for which a TD50 was not available, we estimated the 24-hour airborne exposure directly from the test data. In this case, animals were exposed for 6 hours each day, and this was adjusted downward by multiplying by 6/24.

Carcinogenic risk. We present several estimates of lifetime risks. (1) Maximum likelihood (MLE) and 95% upper confidence interval (UCL) risks were estimated for each indoor air concentration using the multi-stage model as described by Crump (1982), assuming additivity [see Crump (1982) for explanation]. (2) Risks were also calculated from the most potent TD50 (Peto, et al., 1984; Sawyer, et al., 1984) estimated by Gold, et al (1984,1986). We have assumed this value is a point on a linear dose response curve, and have divided 0.5 by the TD50 (estimated as the equivalent dose in ug/m^3) to obtain the risk per unit dose. When Gold, et al (1984,1986) reported that curves were non-linear we have indicated this by modifying the risk estimate with a 'less-than'(<) or 'greater-than'(>) sign. (3) EPA estimates are presented as 95% UCL risks and were calculated from the unit-risk values for exposure to a lifetime airborne concentration of 1 ug/m^3 (Anderson, et al., 1983; EPA, 1985, 1985a-f, 1986), assuming linearity.

RESULTS

Risk from exposure to individual compounds.

The ratio of TD50 to indoor exposure. The difference between exposures producing cancer in the animal tests and the actual human exposures in indoor air is of interest as an indication of: (1) Whether any carcinogens are present at sufficiently high concentrations to produce effects that may be experimentally observable; and (2) the ranges over which uncertain extrapolation models must be applied to estimate risk. These were approximated by tabulating the ratio of the adjusted TD50 to indoor air concentrations (Table 2). The TD50 and actually administered doses may vary by a factor of as much as about thirty (Bernstein, et al., 1985). Several points are

apparent from examining these ratios.

Most striking is the similarity of the 'human-equivalent' TD50 (1247 ug/m3) to concentrations of formaldehyde to which some humans may be chronically exposed. Some measurements in non-UFFI homes have actually exceeded this value (see Table 1). However, since considerable irritation would be expected at such concentrations a more realistic upper limit estimate of a concentration to which long term exposures might conceivably occur may be the HUD standard for mobile homes (500 ug/m3). We have used this to obtain the 'Maximum' ratio reported in Table 2.

The choice of a reasonable upper limit for chronic exposure is complex. Because of the decay rate of formaldehyde (half life = 4 years) the HUD standard may be too high. Most new homes would presumably meet the standard, and then show a decrease in concentration over time. On the other hand the HUD standard is only a design standard. Individual mobile homes are not tested for compliance and measurements higher than 500 ug/m3 have been reported, as shown in Table 1. Thus, 500 ug/m3 may not be an unreasonable upper limit estimate.

The HUD standard is only 2-3 times less than the 'human-equivalent' TD50. This is certainly within the range over which dose response effects have been demonstrated in animal cancer tests. There is a great deal of continuing discussion as to whether a threshold (practical or theoretical) exists for formaldehyde carcinogenesis. We will not reproduce that discussion here. The main point we wish to make is that such considerations do not have great impact on the key observation that at least some individuals may be exposed chronically to concentrations of formaldehyde that are within an order of magnitude of the actual doses that have produced cancer in animals. Thus, they may be within the range of observable dose response.

The ratios for most other carcinogens are much greater than for formaldehyde. Ratios for only 4 chemicals are <100. These are: chlordane (28); vinylidene chloride (43); heptachlor (56); and tetrachloroethylene (81). The concentrations for chlordane and heptachlor may be not unreasonable upper limit estimates of some long term exposure situations. Though the measurements in Table 1 were made relatively soon after termiticide treatment, these compounds are known to remain active for long periods (30 years and perhaps longer) (U.S. Air Force, 1982). However, the number of people exposed to such concentrations is probably not large since the great majority of airborne measurements have been far below the maximum values listed. We do not have a mean or median estimate available.

The evidence for carcinogenicity of vinylidene chloride is limited. It appears to be a weak carcinogen in rodents, and the

effect is marginal. Though the chemical is found indoors, it appears to be primarily an outdoor pollutant. It is not frequently detected in homes, though in a very small number of cases relatively high concentrations have been reported. We do not know if these would be expected to occur chronically. If such chronic exposures do occur, provided the limited animal data are correct, risk in these homes could be substantial.

Tetrachloroethylene appears to have both indoor and outdoor sources. Its major indoor use is as a cleaning solvent, and the widely varying concentrations measured suggest intermittent use, as might be expected. Thus, the maximum concentration in the Table is most likely not representative of a chronic exposure situation. The mean concentrations reported for both vinylidene chloride and tetrachloroethylene are much lower than the maximum values, and yield ratios of 420 and 13,000 respectively.

In summary, if carcinogenic potential is examined only from this perspective - that is, only from a consideration of whether we are exposed to any carcinogens at concentrations that might be within an observable dose-response range - then the conclusion must be that the carcinogen for which this is most clearly true is formaldehyde. For several other carcinogens the data are suggestive, but more detailed information on chronic exposures are needed to make a definitive assessment.

Estimates of Individual Risk. In Table 3 are four estimates of lifetime cancer risk from continuous exposure to the maximum or mean concentrations of the 24 carcinogens. Except as indicated in the Table footnote, the estimates derived from the multi-stage model [labeled maximum likelihood (MLE) and 95% upper confidence limit (UCL)], and from the TD50 were all calculated from the dose-response data used by Gold, et al (1984, 1986) to estimate the TD50 that was the most potent among the experiments analyzed. The MLE and UCL estimates are not strictly comparable to the TD50 estimate however, because Gold, et al used lifetable data, and we used summary data in the multi-stage model. The column labeled "EPA" was calculated directly from published EPA unit-risk (risk from exposure to 1 ug/m^3) values (Anderson, 1983; EPA, 1985, 1985a-f, 1986) assuming linearity.

In most cases, the multi-stage MLE is either the lowest estimate, or similar to the lowest estimate. Also, the MLE, and the TD50-derived estimates are quite similar, which agrees with the observation that most of these curves are consistent with linearity (Gold, et al., 1984, 1986). For only 3 chemicals (1,1-dichloroethane, formaldehyde, and heptachlor) do these two estimates differ by more than a factor of 10. In these 3 cases, the MLE is much lower than the TD50-derived estimate. For formaldehyde and heptachlor this is probably due primarily to the non-linearity of the dose-response curves. For 1,1-dichloroethane the reason is less clear, for as Gold, et al

(1984) report, the dose response is consistent with a linear model when lifetable data are used. It is even linear using only the summary data (L. Gold, personal communication). We have not examined the reason for differences between our UCL(95%) estimates and those of EPA. None differ by more than an order of magnitude. These differences almost certainly reflect relatively minor differences in the analyses, such as dose response data or species scaling factors.

The MLE lifetime risk estimates for seven carcinogens (benzene, chlordane, dichloromethane, formaldehyde, lindane, tetrachloroethylene, and vinylidene chloride) are $>10^{-3}$ at the maximum recorded indoor air concentrations. Chlordane was discussed in the previous section. Lindane has led to contamination problems in homes treated with wood preservatives (Van der Kolk, 1984; Gebefugi & Korte, 1984), and has been found in the air of homes even months after treatment at concentrations as high as 40 ug/m^3 (Van der Kolk, 1984). Though undergoing regulatory review (EPA, 1983), it is still a widely used pesticide. EPA assessed risk from a variety of exposures, including those resulting from a number of household uses (EPA, 1979). Several of these resulted in quite high lifetime risks. For example, estimated lifetime risk from waxing household floors every 3 weeks was 2.16×10^{-3}, and from use of treated shelf paper was 1.19×10^{-4}. The estimates we quote in Table 3, ranging from $2.5\text{-}4.1 \times 10^{-3}$, were calculated based on maximum levels found some months after treatment with a wood preservative, making the assumption these levels might be considered an upper limit for chronic exposure. Since lindane is less persistent than most other chlorinated hydrocarbon insecticides this is most certainly an oversimplification. The risk calculated from mean exposures is considerably less ($0.83\text{-}1.4 \times 10^{-5}$).

Estimates for dichloromethane are among the highest in Table 3, both at maximum and mean or median concentrations. It is unclear whether concentrations in the range of the maximum listed in Table 1 (5000 ug/m3) would occur chronically. Unfortunately, we have measurements on dichloromethane from only one study (DeBortoli, et al., 1985) involving 15 homes. The range of dichloromethane concentrations among these homes was very large, more than a factor of a thousand, and levels higher than 1000 were found in only 2 of the 15 homes studied. Common sources of dichloromethane are paint, paint strippers, and spray cans. The high concentrations observed by DeBortoli could reflect the coincidence of occasional usage close to the time measurements were made. These levels are far higher than the highest measurements made in outdoor air [e.g., EPA reports about 50 ug/m^3 as a maximum annual average to which people may be exposed who live near dichloromethane production facilities (EPA, 1985g)].

The high concentrations measured by DeBortoli are much lower than those resulting from use of such common sources of dichloromethane as paint strippers and aerosol spray paints (Girman and Hodgson, 1986). For example, average concentrations in the breathing zone during paint stripping are about 3.5 x 106 ug/m3, and use of aerosol spray paints results in concentrations averaging about 1.4 x 106 ug/m3. These concentrations are hundreds of times the highest levels recorded by DeBortoli. Though these activities are usually engaged in for relatively short periods of time, regular usage would impact significantly on chronic exposure patterns, and could substantially increase risk.

It is difficult to exclude the possibility that some chronic indoor exposures to benzene, tetrachloroethylene, and vinylidene chloride might approach the maximum levels listed in Table 1. For benzene, even the maximum concentrations measured in indoor air are well below human odor and irritation thresholds. These are, respectively, 2x104 ug/m3 (Verschueren, 1983) and 8x104 ug/m3 (Fishbeck, et al., 1978). Based on doses toxic in animal studies, this is probably also true for tetrachloroethylene and vinylidene chloride. Mean or median exposures are much less than the maximum values (the average ratio is 88), though for all three of these chemicals, the risk, even at mean concentrations, is >10-5. This risk, though not totally insignificant, is very small relative to risk at the maximum concentrations. Thus, the most important question to answer is what fraction of the population is exposed to relatively high concentrations for long periods of time. We have addressed this question in a preliminary way in the next section.

Based on the TD50, the mean lifetime risk for formaldehyde is 950 x 10-5, by far the largest cancer risk estimated from mean exposures. The risk estimated at the upper 95% confidence limit using the multi-stage model also places formaldehyde well ahead of the other carcinogens on the Table. Risks from dichloromethane, benzene, and vinylidene chloride exposure rank second on this scale - 6- 9 times less than formaldehyde. The MLE estimate for formaldehyde risk - 0.37 x 10-5 - is 180 times less than the estimate at the 95%UCL, and one of the smallest mean risks. This dramatic difference is most likely due to the extreme non-linearity of the carcinogenesis dose-response in the rat tests, which is fully taken into account by the MLE estimate, but not by the linear extrapolation from the TD50.

Estimating the Fraction of the Population at High Risk.

For benzene, formaldehyde, and 3 other carcinogens we have estimated what fraction of the population may be at relatively high risk. For this exploratory exercise, we have utilized the house-by-house concentration data from a 15-home study (DeBortoli,et al, 1985), and have calculated the per cent of the exposed population in these homes that would be expected to be at

greater than 1 in a thousand lifetime risk of cancer. Results of these calculations are in Table 4.

We have made 3 estimates of the concentration of each compound required for a risk of 10^{-3}: the maximum likelihood (MLE); the corresponding 95% lower confidence interval estimate (LCL); and an estimate calculated from the TD50, assuming linearity. All 3 estimates suggest that 1% or more of the population are at $>10^{-3}$ risk from exposure to benzene. The estimates for formaldehyde vary from an extremely small fraction up to more than 99% of the population.

If the geometric standard deviations of indoor concentrations of various carcinogens are similar, the results of this type of analysis, in terms of the relative hazard attributable to the different chemicals, will not be in disagreement with the analysis based only on mean risks (Table 3). However, as seen by comparing Tables 3 and 4, ranking the chemicals based on the fraction of people at high risk can be strongly dependent on the breadth of the concentration distributions of different chemicals. For example, using the MLE estimates in Table 3, the ratio of risks from exposure to trichloroethylene and carbon tetrachloride are: 1.9 using the maximum concentrations; and 0.44 using the mean or median concentrations. Thus, based on the maximum or the mean values, the risks from exposure to trichloroethylene and carbon tetrachloride do not differ greatly, varying over a range of only about 4. However, a very different picture of the ratio of risks is seen when calculated from the values presented in Table 4. Thus, the MLE risk from exposure to trichloroethylene is 0.014%; and the z-value of 5.67, for risk from exposure to carbon tetrachloride, corresponds to a risk of about 7.1×10^{-7}. The ratio of these is almost 20,000, leading to a very different picture of the relative risks from exposure to these two chemicals. This is because the geometric standard deviation for trichloroethylene (3.47) is much greater than that for carbon tetrachloride (1.87).

Similarly, depending on the degree to which the standard deviations differ, the relative risks of other chemicals will also be affected. Another example are benzene and formaldehyde. Based on the 95% confidence limit estimates of risk from exposure to mean concentrations in Table 3, the risk from formaldehyde exposure is about 10 times that from benzene exposure. However, using the 95% confidence interval values in Table 4, benzene poses a high risk to 3 times more people than formaldehyde. This difference is due to the relatively narrow distribution of formaldehyde among the DeBortoli homes as compared to benzene.

Overall Carcinogenic Risk

The material presented in Tables 2-4 refers to risk from

exposure to individual chemicals, whereas in the indoor environment, exposures are to mixtures of chemicals. This raises the immediate question of the basis for estimating the total risk. Though synergistic or inhibitory effects between carcinogens have been observed in a few instances, there is insufficient knowledge of such interactions to adopt any model for combined effects. Furthermore, even for classes of chemicals for which an additive model might be appropriate (e.g., chemicals with similar mutagenic mechanisms), the biological basis for additivity is insufficient to justify use of such a model without building in substantial uncertainty. Nevertheless, additivity is the first order expectation, and in what follows, we have assumed that the total risk is equal simply to the sum of the individual risks.

Below we have looked at overall carcinogenic risk in two ways. First, we have estimated total mean risk, and secondly we have examined the distribution of risk among exposed populations.

Total Mean Risk. We used the simple additivity model to sum mean risks estimated for each individual carcinogen, where such information was available [mean indoor concentration data were not available for almost all the pesticides in Table 1, nor for dimethylnitrosamine, N-nitrosopyrrolidene, and PCB's]. This was done for the risks presented in Table 3, yielding totals for mean lifetime risk of 28-980 x 10^{-5}. This approximately 40-fold range is primarily caused by the large discrepancies in the estimates for formaldehyde risk, as already discussed. Using the high estimate (950 x 10^{-5}), the risk is dominated by formaldehyde and is about 1 in 100. If the smallest estimate (0.37 x 10^{-5}) is used the overall risk drops precipitously, to roughly 1 in 5000, and formaldehyde is one of the smaller risks, approximately 15 times less than dichloromethane or benzene.

The Distribution of Risk. The concentrations of 7 carcinogens measured by DeBortoli were used to examine total risk on a house-by-house basis. These results are in Table 5. As evident from the coefficients of variation (CV = standard deviation/mean), the distribution of risk across homes for most of the carcinogens is broader than the distribution of total risk from all chemicals combined. shown at the bottom. The CV for the individual chemicals ranges from 51-210%, but for all chemicals combined the CV is 52%. There are two factors which produce this effect. First, if the chemicals present were strongly correlated, the CVs for individual and total risks would be similar. The fact that they are not suggests that many of the chemicals are independently distributed, leading to differences in the individual CVs and to a smaller variance in the total risk. Second, the most broadly distributed chemicals do not contribute very much to the overall risk, which tends to be dominated by formaldehyde and benzene. Thus, it is primarily the

fact that these 2 chemicals are not strongly correlated which leads to the smaller overall CV. [We note that dichloromethane and chloroform are significantly correlated (data not shown).]

DISCUSSION

In this study we have taken a broad overview of possible carcinogenic risks from exposure to organic chemicals in indoor air. We have used several approaches to compare risks from different chemicals, and we have also briefly addressed the question of overall risk. The exposure data available to us were very limited, and so therefore, is the analysis. Nevertheless, there are several points that emerge which may be of interest.

Overall risks from organic chemicals as compared to other cancer risks. We used the simple additivity model to sum mean risks estimated for each of the 24 carcinogens examined (Table 3). The total ranged between 28-980 x 10^{-5}, roughly 1 in 100 to 1 in 4,000, depending upon which of the 4 risk estimates are summed. The 40-fold difference between these estimates is caused primarily by the large discrepancies in estimates for formaldehyde risk (discussed further below). It is difficult to know how much meaning to attach to these estimates, considering uncertainties associated with the individual risk estimates and with the simple addition of risks. Nonetheless, it is of interest to compare these figures with the total risk of actually getting cancer, or with the risk of getting a particular kind of cancer. The total lifetime risk of getting cancer is about 1 in 4. Lung cancer, one of the most common types of cancer, and the one of most obvious concern for exposure from inhalation, has an age-adjusted rate, in white males, of about 1 in 1000 per year (Pitot, 1986). Over a 70 year lifespan this is about 1 in 13. The total lifetime cancer risk summed for the 24 carcinogens in Table 3 is 0.35-13% of this value.

For further comparison, the average lifetime incidence of lung cancer due to indoor radon is estimated to be about 1 in 300 (Nero, et al., 1986), which is comparable to the higher estimates for the organic chemicals, and about an order of magnitude greater than the low estimate. It is important to note that the uncertainty in the risks from organic compounds is substantially larger than uncertainty in the radon estimate. This is because of fragmentary information on exposures and because of the need, in most cases, to make large extrapolations from animal data (factors of 60 to 10,000 as shown in Table 2). In contrast, the radon exposures have an uncertainty of only about 30% and require extrapolation over only a factor of 5 from exposures where effects have been observed. Another important difference is that the observed effects from radon (actually its decay products) are lung cancers among human populations (i.e., various miner groups)

rather than in laboratory rodents. Though interpretation of these human studies requires consideration of potential confounding factors such as smoking or other substances in mine air, the preponderance of evidence yields a risk factor that is thought to be uncertain by only a factor of two or three (NCRP, 1984).

Formaldehyde. There is a 2600-fold difference among the four mean risk estimates presented in Table 3. The maximum liklihood (MLE) estimate is the smallest, 0.37 x 10^{-5}, and the linear extrapolation from the TD50 is the largest, 950 x 10^{-5}. This discrepancy is most likely primarily due to the nonlinearity of the carcinogenesis dose-response curve in rats, which is so pronounced as to produce this discrepancy even over the relatively small extrapolation range (a factor of 23: see Table 2). This nonlinearity is also reflected in the quite large difference between the MLE estimate and its upper 95% confidence limit of 67 x 10^{-5}. For several reasons it is important that we do not dismiss these higher estimates on the grounds that they do not fully take into account the nonlinearity of the rat dose-response. First, because of the high order of non-linearity, the MLE estimate is extremely non-robust, which is to say that it would be very different if only a few more or less tumors had been observed. Since there are only 4 points (including the control) on the dose-response curve, its exact shape is very poorly defined, and consequently the MLE estimate is highly uncertain. Second, there is no reason to believe that there will be similar degrees of non-linearity of the formaldehyde dose response in humans and rats. On the contrary, since a great deal of the non-linearity in the rat curve is due to the protective effect of a muco-ciliary clearance system (Swenberg, et al., 1985) (which humans do not have), one might expect the curve would be much less non-linear in the human. Thus, from this point of view the higher estimates may be more realistic than the MLE estimate.

Finally, it is useful to consider how the risk estimates in Table 3 compare with the lifetime rate of nasal cancer in the U.S. population and with results of epidemiological studies on populations exposed to higher than average levels of formaldehyde. (It is not certain that human cancers due to formaldehyde would necessarily be nasal cancers, though given the high chemical reactivity of formaldehyde it would not be surprising if this were true.) The lifetime incidence of nasal cancer in the U.S. has been reported to be 23-45 x 10^{-5} (CPSC, 1982). If most nasal cancers are due to formaldehyde exposure, this is comparable with the upper confidence interval estimates of risk (67 x 10^{-5}) from lifetime exposure to the mean concentrations of formaldehyde in Table 3. In contrast, the MLE estimate yields a rate that is 62-120 times less than the

observed U.S. rate.

Several recent epidemiological studies have found higher than expected incidences of nasal cancer in different populations exposed chronically to formaldehyde (Blair, et al., 1986; Hayes, et al., 1984; Olsen and Jensen, 1984). In all of these studies, though a higher than expected incidence of nasal cancer was observed, the association was not significant. The interpretation of the results is also complex for other reasons. For example, in two of the studies the observations were confounded by concurrent exposure to wood dust (known to cause nasal cancer), though an increase in nasal cancer remained elevated when the analysis was controlled for wood dust (Hayes, et al., 1984; Olsen and Jensen, 1984). In the Blair, et al. (1986) study, there was a deficit for cancer of the buccal cavity and pharynx combined, but the data (see Table 5 in Blair, et al) indicate a more than 3-fold increase over expected rates in the exposed population when the nasopharynx is examined separately. Though these results are only suggestive, the fact that all three studies have independently found some association between nasal cancer and formaldehyde exposure is of interest. Without more knowledge of the age structure of the study populations it is not possible to compare the results of these studies with that predicted from the risk estimates in Table 3. However, we may make a rough comparison by considering only the high exposure category. For example, in the Blair, et al study about 1,000 workers were considered at risk from chronic exposures higher than 2,000 ug/m3. If we assume these are 6 hour exposures and adjust them to the equivalent 24-hour values (500 ug/m3), the UCL estimate of 9.3 x 10-3 from Table 3 would suggest that, if these workers were exposed for a lifetime, (9.3x10-3)(1,000) = 9 cancers would occur. Since the Blair, et al study only considered causes of mortality, and the risk estimate is of expected incidence, we might assume approximately a 50% cure-rate, adjusting the estimate downward to 4-5 expected cases. Since workers were not observed for their lifetimes, this number is still too high. Blair, et al did not observe any nasal cancers among this high exposure group. This may not be inconsistent with the prediction from the UCL estimate, and it seems worthwhile to examine this point more carefully using the lifetable data.

In sum, the formaldehyde case is complex, as many others have discussed (e.g., Anon, 1984; Swenberg, et al., 1985). Formaldehyde is an ubiquitous indoor pollutant, and it appears likely that it is present in some homes at concentrations that are not very far from doses that have produced cancer in rodents. It is important to refine the risk estimates to determine if formaldehyde is responsible for most of the cancer risk (as suggested by the highest estimates), or a relatively small per cent of the risk (as suggested by the lowest estimates), or a significant, though not dominant fraction (as suggested by the

UCL estimates). Based on the considerations discussed here, the UCL estimates appear, at least currently, to be the least problematic as they neither ignore nor overinterpret the poorly defined non-linear dose-response in rats, and they do not incorporate the assumption that the dose-response in humans will be as non-linear as in rats.

Concentration distributions and risk estimation. The data presently available on concentrations of chemicals in the indoor environment are meager. For virtually no chemical do we have sufficient direct information to state what the frequency distribution of concentrations is, nor are we able to cite average exposures with much accuracy. The limitations of information available from monitoring is evident from the data given in Table 1, where, in most cases few measurements have been performed, sometimes in circumstances where concentrations are expected to be far higher than average. Even in the best examples, the averages cited can be used for assessment purposes only with great uncertainty.

The principal exception to these generalizations about organic compounds is formaldehyde, of which many measurements have been performed in a variety of indoor environments (e.g., see Anon, 1984 for a summary). The distribution of formaldehyde concentrations is skewed toward high concentrations, and is approximately a log normal distribution. This has also been observed for radon (Nero, et al., 1986), and frequency distributions for other chemicals involving smaller numbers of homes are not inconsistent with this picture (e.g., Lebret, 1985; Hawthorne, et al., 1984).

Knowledge of the distribution is extremely important in cancer risk assessment, because it permits one to estimate what fraction of the population is at relatively high risk. Risk assessments that involve multiplying extremely small estimates of individual risk (usually calculated assuming some mean exposure level) by extremely large numbers of exposed people (e.g., see the EPA risk assessment for formaldehyde exposure in homes - EPA, 1984) may well stretch the limits of extrapolation models beyond what is reasonable. Of much greater scientific credibility are estimates of risk for populations that are exposed to doses of carcinogens that are not too far from the doses that have been observed to actually cause cancer. If adequate exposure distributions are available, such populations can readily be determined. Also, even if data are inadequate to define the form of the distribution, if it possible to say that the overall distributional forms are sufficiently similar to the general form of a lognormal distribution, then the data may be characterized approximately using lognormal parameters. This will permit the construction of a more adequate picture of risk, allowing us to extract the greatest possible information from the data available to us.

As illustrated above, based on comparing Tables 3 and 4, the ranking of carcinogens when risks are estimated based only on mean exposures and, alternatively, when the GSD is taken into account can be dramatically different. It seems an important priority to collect house-by-house concentration data suitable for approximating distributions of carcinogens that appear, by preliminary risk assessment, to pose the greatest hazard.

Comparable considerations apply to assessment of exposures and risk for other health endpoints: a wide range of exposures exist, and in some cases the dose-effect relationship may be even more complicated than for carcinogens, involving threshold and sensitization phenomena. Fuller understanding and evaluation of the health effects of chemicals in the indoor environment will require more complete information from surveys yielding exposure distributions and from studies examining dose-effect relationships.

ACKNOWLEDGMENTS

This work was supported by the Director, Office of Energy Research, Office of Health and Environmental Research, Human Health and Assessments Division of the U.S. Department of Energy under Contract No. DE-AC03-76SF00098.

REFERENCES

Anderson, L.A. (1983). "Quantitative Approaches in Use to Assess Cancer Risk," Risk Analysis, 3, p. 277-295.

Anon. (1984) "Report on the consensus workshop on formaldehyde," Env. Health Persp. 58, pp. 323-381.

Beall, J.R. and Ulsamer, A.G. (1981). "Toxicity of Volatile Organic Compounds Present Indoors," Bull. N.Y. Acad. Med. Vol. 57, No. 10, pp. 978-996.

Berglund, B., Johansson, L. and Lindvall, T. (1982). "A Longitudinal Study of Air Contaminants in a Newly Built Preschool," Environmental International, Vol. 8, pp. 111-115.

Bernstein, L, L.S. Gold, B.N. Ames, M.C. Pike and D.G. Hoel (1985) Some tautologous aspects of the comparison of carcinogenic potency in rats and mice. Fund. Appl. Toxicol. 5:79-86.et al (1985) - TD50/LD50 ariticle.

Blair, A., P. Stewart, M. O'Berg, W. Gaffey, J. Walrath, J. Ward, R. Bales, S. Kaplan, D. Cubit (1986) "Mortality among industrial workers exposed to formaldehyde", J. Natl. Cancer Institute 76:1071-1084.

CPSC (1982) "Ban of urea-formaldehyde foam insulation", Federal Register 47:14366-14419.

Crump, K.S. (1982) "An improved procedure for low-dose carcinogenic risk assessment from animal data", J. of Environ. Pathol. and Toxicol. 5:675-684.

Dave, J.M. (1984) "Studies on emissions from coal burning stoves (sigries) as used in eastern India," School of Envir. Sciences, Jawarharlal Nehru University, New Delhi, India, pp. 383-388. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

De Bortoli, M., Knoppel, H., Pecchio, E., Peil, A., Rogora, L., Schauenburd, H., Schlitt, H., and Vissers, H. (1985). Measurements of indoor air quality and comparison with ambient air. EUR 1656 EN, Directorate-General for Science, Research and Development, Joint Research Center.

Deshpande, J.M., Nayak, U.V., Nayak, S.U. and Patwardhan, J.R. (1984). "Indoor air quality in Bombay, India with respect to respirable particulates, benzo(a)pyrene and sulphates," Air Quality Monitoring and Research Laboratory, Municipal Corporation of Greater Bombay, Bombay, India. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

EPA (1979). The Carcinogen Assessment Group's risk assessment on lindane, April 20, 1979. Requested by the EPA Office of Pesticide Programs.

EPA (1983) Lindane: Notice of intent to cancel. Federal Register 48:48512.

E.P.A. (1984) Formaldehyde; Determination of Significant Risk; Advance Notice of Proposed Rulemaking and Notice. Federal Register 49:21870-21898. May 23, 1984.

E.P.A (1985a) Health Assessment Document for Tetrachloroethylene (perchloroethylene) final report EPA/600/8-82/005F July, Office of Health and Environmental Assessment. Wash. D.C.

E.P.A. (1985b) Health Assessment Document for Vinylidene Chloride. Final Report. EPA/600/8-83/031F. August, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1985c) Health Assessment Document for Trichloroethylene. Final Report. EPA/600/8-82/006F. July, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1985d) Addendum to the Health Assessment Document for Dichloromethane (Methylene Chloride). Updated Carcinogenicity Assessment of Dichloromethane (Methylene Chloride). EPA/600/8-82/004FF. September, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1985e) Health Assessment Document for Tetrachloroethylene (Perchloroethylene). Final Report. EPA/600/8-82/006F. July, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1985f) Health Assessment Document for 1,2-Dichloroethane (Ethylene Dichloride). EPA/600/8-84/006F. September, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1985g) Health Assessment Document for Dichloromethane (Methylene Chloride). Final Report. EPA/600/8-82/004F. February, Office of Health and Environmental Assessment, Washington, D.C.

E.P.A. (1986) Memo to Richard Hefter from Nancy Pate, dated March 20.

Erikson, P.S., Gennser, G., Lofgren, O., and Nilsson, K. (1983). "Accute Effects of Maternal Smoking on Fetal Breathing and Movement," OBST and Gynec 61, pp. 367-372.

Fishbeck, W.A., Townsend, J.C. and Swank, M.G. (1978). "Effects of Chronic Occupational Exposure to Measured Concentrations of Benzene," J. Occup. Med. 20, pp. 539-542.

Gebefugi, I. and Korte, F. (1984) Indoor contamination of housefold articles through pentachlorophenol and lindane, Proc. of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Girman, J.R. and Hodgson, A.T. (1986) Source characterization and personal exposure to methylene chloride from consumer products.

Presented at the 79th Annual Meeting of the Air Pollution Control Association. Minneapolis, Minnesota, June 22-27. To be published in the Proceeding of the conference.

Gold, L.S., deVeciana, M., Bakeman, G., Magaw, R., Lopipero, P., Smith, M., Blumenthal, M., Levinson, R., Bernstein, L., and Ames, B.N. (1984) "A Carcinogenic Potency Data-Base of the Standardized results of Animal Bioassays," Environ: Hlth. Perspec. 58, pp. 9-319.

Gold, L.S., deVeciana, M., Bakeman, G., Magaw, R., Lopipero, P., Smith, M., Blumenthal, M., Levinson, R., Bernstein, L., and Ames, B.N, (1986). "Chronological Supplement of the Carcinogenic Potency Data Base: Standardized Results of Animal Bioassays Published Through December, 1982," Environ. Hlth. Perspec., vol. 67.

Hartwell, T.D., Perritt, R.L., Zelon, H.S., Whitmore, R.W. and Pellizzari, E.D. (1984a). "Comparisons of Indoor and Outdoor Levels for Air volatiles in New Jersey." Research Triangle Institute, Research Triangle Park, N.C. pp. 81-85. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Hartwell T.D., Zelon, H.S. Leininger, C.C., Clayton, C.A., Crowder, J.H. and Pellizzari, E.D. (1984b). "Comparative Statistical Analysis for Volatile Halocarbons in Indoor and Outdoor Air," Research Triangle Institute, Research Triangle Park, N.C., pp. 57-61. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Hawthorne, A.R., R.B. Gammage, C.S. Dudney, T.G. Matthews, D.J. Erdman (1984) Formaldehyde levels in forty east Tennessee homes. pp17-22 in Volume 3 of Proceedings of the 3rd International Conference on Indoor Air Quality and Climate.

Hayes, R.B., Raatgever, J.W. and DeBruyn, A. (1984) Tumors of the nose and nasal sinuses: A case-control study. Presented at the XXI Congress on Occupational Health, Dublin, Ireland, September 1984.

IARC (1978). Some N-nitroso compounds. Monographs on the evaluation of carcinogenic risk of chemicals to humans. Volume 17.

Johansson, I. (1978). "Determination of Organic Compounds in Indoor Air with Potential Reference to Air Quality," Atmos. Environ. 12, pp. 1371-1377.

Jurinski, N.B. 1984. "The Evaluation of Chlordane and Heptachlor Vapor Concentrations within Buildings Treated for Insect Pest Control" pp. 51-56. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Lebret, E. (1985) Air pollution in Dutch homes. An exploratory study in environmental epidemiology. Department of Air Pollution. Wageningen Agricultural University. The Netherlands. Report R-138. Report 1985-221.

Lebret, E., van de Wiel, H.J., Bos, H.P., Noij, D. and Boleij, J.S.M.

(1984). "Volatile Hydrocarbons in Dutch Homes," Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Matsushita, H. and Mori, T., (1984). "Nitrogen Dioxide and Nitrosamine Levels in Indoor Air and Side-Stream Smoke of Cigarette," pp. 335-340. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

McCann, J., L. Horn, J. Girman, A.V. Nero (1986) Potential risks from exposure to organic compounds in indoor air. Lawrence Berkeley Laboratory. Report LBL-22473.

Molhave, L. (1979). "Luftens indhold af gasafter, dampe og stove i nyere boliger." Ugeskr. Laeg. 141/14, pp. 956-961.

Monteith, D.K. and Stock, T.H. (1984). "Sources and Characterization of Organic Air Contaminants inside Manufactured Housing," pp. 285-290. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

NCRP (1984) Evaluation of occupational and environmental exposures to radon and radon daughters in the United States. NCRP Report No. 78. National Council on Radiation Protection and Measurements, Bethesda, MD.

Nero, A.V., Schwere, M.B., Nazaroff, W.W. and Revzan, L.L. (1986) Distribution of airborne radon-222 concentrations in U.S. homes. Science, Nov. 21.

NTP (1986) NTP Technical Report on the Toxicology and Carcinogenesis Studies of Dichloromethane (Methylene chloride) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). NTP TR306. NIH Publication No. 86-2562.

Olsen, J.H. and Jensen, O.M. (1984) Case-control study on sinonasal cancer and formaldehyde exposure based on a national data linkage system for occupation and cancer. Presented at the Society for Epidemiologic Research, 17th Annual Meeting, Houston, Texas, June 13-15, 1984. Am. J. Epidemiology 120:459.

Pellizzari, E.D., Sheldon, L.S., Sparacino, C.M. and Bursey, J.T. (1984). "Volatile Organic Levels in Indoor Air," U.S. Environ. Protection Agency, Res. Triangle Park, N.C. pp. 303-308. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Peto, R., Pike, M.C., Bernstein, L., Gold, L.S. and Ames, B.N. (1984). "The TD50: A Proposed General Convention for the Numerical Description of the Carcinogenic Potency of Chemicals in Chronic-Exposure Animal Experiments," Environ. Health Persp. 58, pp. 1-8.

Pitot, H.C. (1986). Fundamentals of Oncology. 3rd Ed. Marcel Dekker, Inc. NY.

Reinert, J.C. (1984). Pesticides in the Indoor Environment. Pesticide

Programs, USEPA, Washington, D.C., pp. 233-238.

RTECS (1984). Registry of Toxic Effects Ed. Tatken, R.L. and Lewis, R.J., U.S. Dept of Health and Human Services Cinc. Ohio.
Sawyer, C., Peto, R., Bernstein, L., M.C. Pike (1984) Calculation of carcinogenic potency from long-term animal carcinogenesis experiments. Biometrics 40:27-40.

Seifert, B. (1982) Vergleich der innerhalb und auberhalb geschlossener Raume auftretenden Konzentrationen anorganischer und organischer Verbindungen. In: K. Aurand, B. Seifert, and J. Wegner (Eds.). Luftqualitat in Innenraumen. Gustav Fischer Verlag, Stuttgart, pp41-74.

Sexton, K. (1984). "The Effects of Residential Wood Combustion on Indoor and Outdoor Air Quality: A Case Study in Waterbury, Vermont," Calif. Dept. of Health Services, Berkeley, CA., pp. 111-116. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Swenberg, J.A., H. d'A. Heck, K.T. Morgan, and T.B. Starr (1985) A Scientific Approach to Formaldehyde Risk Assessment. In Risk Quantitation and Regulatory Policy. Banbury Report 19. Eds. D.G. Hoel, R.A. Merrill, F.P. Perera, Cold Spring Harbor Laboratory.

Thyssen, J., Althoff, J., Kimmerle, G., and Mohr, U. (1981). JNCI 66, pp. 575-577.

Turiel, I., Hollowell, C.D., Miksch, R.R., Rudy, J.V., Young R.A. and Coye, M.J. (1981). The Effects of Reduced Ventilation on Indoor Air Quality in an Office Building. Lawrence Berkeley Laboratory, Energy and Environment Division, pp. 1-48.

U.S. Air Force (1982) Chlordane in Air Force JFamily Housing -- A study of houses treated prior to construction. United States Air Force Occupational and Environmental Health Laboratory, Aerospace Medical Division, Brooks Air Force Base, Texas.

Van Der Kolk, J. (1984) Wood preservatives and indoor air; experiences in the Netherlands. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden. pp251-256.

Vedel, A., and Nielsen, P.A. (1984). "Phthalate Esteres in the Indoor Environment," pp. 309-314. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Verschueren, K. (1983). Handbook of Environmental Data on Organic Chemicals. 2nd Ed. Von Nostrano Reinbold Co. NY, NY.

Wallace, L. (1984). "Analyses of Exhaled Breath of 355 Urban Residents for Volatile Organci Compounds," U.S. Environ. Prot. Agency, Washington, D.C. pp. 15-20. Proceedings of the 3rd International Conference on Indoor Air Quality and Climate, Stockholm, Sweden.

Wallace, L., (1982). "Monitoring Individual Exposure. Measurements of

Volatile Organic Compounds in Breathing-Zone Air, Drinking Water, and Exhaled Breath" Enviorn. Intern. 8, pp. 269-282.

Wang, T.C. (1975). "A Study of Bioeffluents in a College Classroom," ASHRAE Trans. 81, (Part 1), pp. 32-44.

Wanner, H-U. and Kuhn, M. Indoor Air Pollution by Building Materials. Dept. of Hygiene and Applied Physiology, Zurich, Switzerland., pp. 35-40.

Table 1. Indoor Concentrations of Organic Chemical Carcinogens

CHEMICAL	RTECS#[1]	TYPE[2]	N[3]	CONCENTRATION (ug/m^3)[4] Maximum	Median or Mean	REFERENCE
Aldrin	IO21	H	6	0.550	-	Reinert, 1984
Benzene	CY14	H	15	204.0	35.0	DeBortoli, et al., 1985
		H	134	150.0	9.9	Lebret, et al., 1984
		H[5]	355	54.0	16.0	Wallace, et al., 1984
		H	NS	50.0	-	Seifert, 1982
		H[5]	85	120.0	13.0	Hartwell, et al., 1984b
		P	2	36.0	12.0	Pellizzari, et al., 1984
		P	2	27.0	6.1	"
		C	1	27.0	18.0	Turiel, et al., 1981
		PM	17	387.0	4.6	Wallace, et al., 1982
Benzo[a]pyrene	DJ3675	H	6	0.0034	0.0007	Sexton, et al., 1984
		H	NS	0.0607	0.0135	Deshpande, et al., 1984
		H	NS	0.030	-	Seifert, 1982
Carbon tetrachloride	FG49	H	15	12.0	7.0	DeBortoli, et al., 1985
		H	134	0.40	<0.4	Lebret, et al., 1984
		H[5]	355	5.7	1.5	Wallace, et al., 1984
		H[5]	20	13.0	0.17	Hartwell, et al., 1984a
		H[5]	27	17.0	0.075	"
		H[5]	11	3.8	1.3	"
		H[5]	85	14.0	1.4	Hartwell, et al., 1984b
		P	6	0.64	0.41	Pellizzari, et al., 1984
		P	6	3.0	0.86	"
		C	1	-	<1.0	DeBortoli, et al., 1985
Chlordane	PB98	H	NS	10.0	-	Beall & Ulsamer, 1981
		H	4800	40.0	-	Reinert, 1984
		H	9	3.2	-	Jurinski, 1984
Chloroform	FS91	H	15	15.0	<1.0	DeBortoli, et al., 1985

		H[5]	355	17.0	3.4	Wallace, et al., 1984b
		H	NS	200[6]	-	Seifert, 1982
		H[5]	20	26.0	3.7	Hartwell, et al., 1984a
		H[5]	27	6.4	0.008	"
		H[5]	11	47.0	7.6	"
		H[5]	85	215.0	2.9	Hartwell, et al., 1984b
		P	6	3.1	1.7	Pellizzari, et al., 1984
		P	6	2.6	1.1	"
		C	1	-	<1.0	DeBortoli, et al., 1985
		PM	17	17.5	4.0	Wallace, et al., 1982
Dibenz[a,h]anthracene	HN2625	H	6	0.0005	0.0001	Sexton, et al., 1984
1,2-Dibromoethane	KH9275	PM	17	<0.14[7]	-	Wallace, et al., 1982
1,1-Dichloroethane	KI0175	PM	17	1.8	0.06	Wallace, et al., 1982
1,2-Dichloroethane	KI0525	H[5]	20	15.0	0.025	Hartwell, et al., 1984a
		H[5]	27	69.0	3.6	"
		H[5]	11	4.7	0.04	"
		PM	17	12.8	0.58	Wallace, et al., 1982
Dichloromethane	PA805	H	15	5000.0	225.0	DeBortoli, et al., 1985
		C	1	-	<10.0	DeBortoli, et al., 1985
Dieldrin	I0175	H	12	0.47	-	Reinert, 1984
Di(2-ethylhexyl)phthalate	TI035	P	NS	230.0	<60.0	Vedel & Nielsen, 1984
Dimethylnitrosamine	IQ0525	H	NS	0.8[8]	-	Seifert, 1982
		H		-	<0.005[9]	IARC, 1978
		P		0.24[10]	-	"
		P	NS	0.061	-	Matsushita & Mori, 1984
		P	NS	0.066	-	"
Ethanol	KQ63	H	46	550.0	385.0	Molhave, et al., 1979
		H	NS	-	50.0	Seifert, 1982
		P	1	66.0	-	Johansson, 1978

		P	1	85.0	71.0	Wang, 1975
		P	1	-	4.2	"
Formaldehyde	LP8925	H	15	52.0	26.0	DeBortoli, et al., 1985
		H	41	124.0	37.0	Anon, 1984
		H	378	124.0	43.0	"
		H	40	-	74.0	"
		H	64	136.0	62.0	"
		H		255.0	77.0	Hawthorne, et al., 1984
		P		>372.0	58.0	"
		P	6	112.0	87.0	Berglund, et al., 1982
		C	1	-	35.0	DeBortoli, et al., 1985
		M	431	3720.0	471.0	Anon, 1984
		M	50	372.0	124.0	"
Heptachlor	PC07	H	NS	1.8	-	Reinert, 1984
		H	9	15.0	-	Jurinski, 1984
Lindane	GV49	H	NS	50.0	-	Van der Kolk, 1984
N-Nitrosopyrrolidine	UY1575	P	NS	0.036	-	Matsushita & Mori, 1984
		P	NS	0.027	-	"
PCB's (all isomers)	TQ135-1376	H	NS	0.5	-	Seifert, 1982
Styrene	WL3675	H	355	4.6	1.8	Wallace, et al., 1984
		H^5	85	54.0	1.8	Hartwell, et al., 1984b
		M	44(30)	36.0	3.0	Monteith, et al., 1984
		PM	1	13.0	8.5	Pellizzari, et al., 1984
		PM	1	3.2	1.4	"
Tetrachloroethylene	KX385	H	15	64.0	13.0	DeBortoli, et al., 1985
		H	134	205.0	4.1	Lebret, et al., 1984
		H^5	355	26.0	6.4	Wallace, et al., 1984
		H^5	20	28.0	1.6	Hartwell,et al., 1984a
		H^5	27	69.0	0.4	"
		H^5	11	34.0	2.5	"
		H^5	85	250.0	5.6	Hartwell, et al., 1984b

		P	2	7.3	2.1	Pellizzari, et al., 1984
		P	2	98.0	3.3	"
		C	1	-	3.0	DeBortoli, et al., 1985
		M	44(27)	103.0	6.3	Monteith, et al., 1984
		PM	17	718.0	5.9	Wallace, et al., 1982
Trichloroethylene	KX455	H	15	112.0	12.0	DeBortoli, et al., 1985
		H	NS	50.0	-	Seifert, 1982
		H	134	106.0	<1.5	Lebret, et al., 1984
		H[5]	355	12.0	2.3	Wallace, et al., 1984
		H[5]	20	2.0	0.096	Hartwell, et al., 1984a
		H[5]	27	6.4	0.075	"
		H[5]	11	1.3	0.86	"
		H[5]	85	47.0	2.0	Hartwell, et al., 1984b
		P	2	1.9	0.67	Pellizzari, et al., 1984
		P	2	70.0	4.9	"
		C	1	10.0	8.5	Turiel, et al., 1981
		C	1	-	3.0	DeBortoli, et al., 1984
		PM	17	182.0	5.4	Wallace, et al., 1982
Vinylidene chloride	KV9275	H[5]	27	12.0	0.015	Hartwell, et al., 1984a
		PM	17	416.0	5.3	Wallace, et al., 1982

[1] RTECS, 1982,1984.

[2] H = home; P = public building; C = complaint building; M = manufactured home; PM = personal monitor.

[3] N indicates the number of buildings in which measurements were made. When measurements were below the detectable limit, we have indicated the number of buildings in which measurements were above the detectable limit in parenthesis.

[4] The number of measurements made in each building varied considerably among the different reports. The specific details are indicated below for each citation. Anon, 1984: Maxima and means are from data in Table 3. Beall & Ulsamer, 1981:Maxima on pesticides are from the text; values in Table 1 were assumed to be ug/m^3; we reported values in Table 1 only if they did not also appear in Molhave, et al., 1979. Berglund, et al., 1982: The large and small room data in Figures 2 and 3 were combined. There were 2 rooms sampled at 3 different times over which the mean was determined. DeBortoli, et al., 1985: Medians and maxima were calculated from Table 1; the medians were determined from 4-7 day averages over 15 homes. In the case of N=1, only the 4-7 day average for one complaint building is given. Deshpande, et al., 1984: Maximum and mean are from Table 7; authors report the mean for 60 samples, but the number of buildings is not specified. Hartwell, et al., 1984a: Since multiple sites were

examined, all 3 medians and maxima in Table 2 were recorded. Hartwell, et al., 1984b: Medians and maxima are from Table 2. Johansson, 1978: Maxima were estimated from Figure 2; data are from one room when occupied and unoccupied. Jurinski, 1984: Data are from Table 2; data in the 'pre-treat' category were considered maxima. Lebret, et al., 1984: Means and maxima in Table 1a were recorded. Matsushita and Mori, 1984: Only office data in Table 3 were used; the number of buildings was not specified. Molhave, et al., 1979: The mean of the medians in Table 2 for 7 new and 39 older buildings were calculated. Monteith, et al., 1984: Means and maxima are from Table 1; manufactured homes were assumed to be mobile homes; there were 3 rooms in one office tower and 5 in another over which we determined a median. Pellizzari, et al., 1984: Data are from Tables 2,3, and 4; medians and maxima were calculated from indoor measurements only; the medians were calculated from several measurements in 2 different buildings. Reinert, 1984: Data are from Tables 3 and 4: measurements made immediately after application were not taken. Sexton, et al., 1984: Data are from Tables 2 and 3; medians were calculated from indoor measurements of 6 buildings measured at 2 different times. Turiel, et al., 1981: Data are from 1 office building repoorted in Tables 4 and 5; data on benzene were not used; a.m./p.m. measurements in Table 4 were taken as replicates; the values we report are the means of the a.m./p.m. measurements in Table 4 and the values reported in Table 5. Van der Kolk, 1984: Data from an unspecified number of buildings are from Table 1. Vedel & Nielson, 1984: Maximum and mean for 3 rooms given in text but number of buildings not specified. Wallace, et al., 1982: Data are from Tables 13 and 14; the number we report is the average of the two medians reported (one median was from a group of 6 people, the other from a group of 11), and the high number of the range. Wallace, et al., 1984: Data are from Table 2; the 90th percentile values were taken as maxima; there were 705 personal samples taken from 355 people. Wang, 1975: Medians were calculated from data in Table 2; we recorded them as maxima because measurements were in new buildings prior to occupancy.

[5] Overnight personal monitor.

[6] Air above an indoor swimming pool.

[7] 1,2-Dibromoethane was not detected in any samples. The value presented is the limit of detection.

[8] In the interior of new motor vehicles.

[9] Average of reports from urban and suburban non-smoker residences.

[10] Maximum and mean of 8 values reported from measurements in smoke-filled public buildings (e.g., bar, discotheque).

Table 2. Ratio of the most potent TD50 to concentrations measured in indoor air.

Carcinogen	Estimated 'Human-Equivalent' TD50 (ug/m^3)[1]	TD50 / CONCENTRATION[2] Maximum	Mean or Median
Aldrin	570	1000	-
Benzene	1.2×10^5	310	8600
Benzo[a]pyrene	8500	1.3×10^5	1.2×10^6
Carbon tetrachloride	8.8×10^4	5200	$<6.3 \times 10^4$
Chlordane	1100	28	-
Chloroform	3.7×10^4	790	$<1.4 \times 10^4$
Dibenz[a,h]anthracene	4500	9.0×10^6	4.5×10^7
1,2-Dibromoethane	1700	$>1.2 \times 10^4$	-
[1,1-Dichloroethane[3]	8.4×10^5	4.7×10^5	1.4×10^7]
1,2-Dichloroethane	8600	124	7800
Dichloromethane[4]	1.8×10^6	355	$<1.5 \times 10^4$
Dieldrin	420	890	-
Di(2-ethylhexyl)-phthalate	3.6×10^6	1.6×10^4	6.0×10^4
Dimethylnitrosamine	180	225	-
Ethanol	1.3×10^7	3.3×10^4	9.9×10^4
Formaldehyde[5]	1247	2.5[6]	23
Heptachlor	840	56	-
Lindane	1.2×10^4	240	-
N-Nitrosopyrrolidine	3300	9.2×10^4	-
PCB's (Aroclor 1260)	1600	3200	-
[Styrene3	2.8×10^5	5200	8.5×10^4]
Tetrachloroethylene	5.8×10^4	81	1.3×10^4
Trichloroethylene	3.2×10^5	1800	$>9.4 \times 10^4$
Vinylidene chloride	1.8×10^4	43	420

[1]Except as indicated, values were calculated from the most potent TD50s reported by Gold, et al (1984,1986)as described in Methods. For 1,2-dibromoethane, formaldehyde, and vinylidene chloride, which were tested via the inhalation route, we estimated the 'human-equivalent' TD50 by converting the value reported by Gold, et al. to ug/m^3 using their species scaling factors. Dichlorvos and malathion were not included, as the experiments from which the TD50s were calculated were considered to be negative by the NCI (Gold, et al., 1984). The NCI/NTP-sponsored bioassay for lindane was also considered negative. The TD50 used was from another study that was positive. 1,1-Dichloroethane and styrene are in brackets because results of the animal bioassays were judged suggestive by the NCI (Gold, et al., 1984).

[2]Except as indicated maxima are from Table 1. The mean is the average of all means or medians reported in Table 1.

[3]The experiment from which the TD50 was calculated was judged suggestive by the NCI (Gold, et al., 1984).

[4]The TD50 has not been calculated by Gold, et al (personal commun.). We have estimated a value as the lowest administered dose resulting in a significant incidence of cancer (NTP,1986) and adjusted for 24-hour

exposure as indicated in Methods.
[5]The most potent TD50 was 0.798 mg/kg/day in male rats. (L.S. Gold., personal commun.).
[6]We have used 500 ug/m^3 as the highest plausible concentration for chronic exposure (see text).

Table 3. Estimates of carcinogenic risk from lifetime exposure to 26 carcinogens in indoor air

Carcinogen	Risk estimated from maximum concentrations ($\times 10^{-5}$)[1]				Risk estimated from mean or median concentrations ($\times 10^{-5}$)			
	MLE	UCL(95%)	EPA	TD50	MLE	UCL(95%)	EPA	TD50
Aldrin	18.0	57.0	NA	48.0	-	-	-	-
Benzene	128.0	207.0	270.0	>160.0	4.6	7.4	9.8	5.7
Benzo[a]pyrene[2]	0.45	0.73	NA	0.4	0.048	0.077	NA	0.042
Carbon tetrachloride	8.1	12.0	NA	9.7	0.66	0.95	NA	<0.8
Chlordane	1300.0	1600.0	NA	1800.0	-	-	-	-
Chloroform[3]	40.0	50.0	NA	66.0	2.2	2.7	NA	<3.6
Dibenz[a,h]anthracene	0.0025	0.0039	NA	0.0055	0.0005	0.00078	NA	0.0011
1,2-Dibromoethane	1.4	1.8	0.84	<4.1	-	-	-	-
[1,1-Dichloroethane[4]	1.1×10^{-7}	0.040	NA	0.11	1.1×10^{-10}	0.0013	NA	0.0035]
1,2-Dichloroethane	62.0	80.0	48.0	<390.0	0.99	1.3	0.77	<6.3
Dichloromethane[5]	180.0	253.0	2100.0	NA	8.1	11.0	120.0	NA
Dieldrin	53.0	110.0	NA	56.0	-	-	-	-
Di(2-ethylhexyl)-phthalate	2.8	4.9	NA	3.2	0.72	1.3	NA	0.84
Dimethylnitrosamine	38.0	67.0	400.0	222.0	-	-	-	-
Ethanol	2.7	4.2	NA	1.4	0.95	1.5	NA	0.46
Formaldehyde[6]	312.0	928.0	650.0	9000.0	0.37	67.0	69.0	950.0
Heptachlor	18.0	410.0	NA	<900.0	-	-	-	-
Lindane	250.0	410.0	NA	>270.0	0.83	1.4	-	>0.97
N-Nitrosopyrrolidine	1.0	1.7	NA	0.54	-	-	-	-
PCB's (Aroclor 1260)	18.0	21.0	NA	15.0	-	-	-	-
[Styrene[7]	8.4	12.0	NA	9.7	0.51	0.76	NA	0.59]
Tetrachloroethylene[8]	130.0	160.0	35.0	620.0	0.79	1.0	0.22	3.9
Trichloroethylene[9]	15.0	20.0	23.0	29.0	0.29	0.39	0.44	<0.54
Vinylidene chloride[10]	1080.0	1600.0	2100.0	1300.0	7.3	11.0	14.0	8.1

[1]MLE and UCL(95%) estimates were calculated as described in Methods using the dose response data given by Gold, et al (1984,1986) corresponding to the experiment yielding the most potent result as measured by the TD50, except as follows: benzene was estimated from exp. number 331; and dimethylnitrosamine from exp. number 2043.

The estimates labeled 'EPA' were obtained by multiplying the EPA unit risk values, as cited, by the appropriate indoor air concentrations from Table 1. The estimate labeled 'TD50' was obtained from the most potent TD50 assigned by Gold, et al (1984, 1986) assuming linearity. Mean indoor air concentrations were determined as indicated in the footnote to Table 2. 1,1-Dichloroethane and styrene are in brackets because results of the animal cancer tests were judged suggestive by NCI (Gold., et al., 1984).

[2]In this study benzo[a]pyrene was administered orally, in the drinking water. Benzo[a]pyrene appears to be at least as potent when administered to hamsters via inhalation (Thyssen,et al., 1981). The lowest effective dose in the inhalation study corresponded to 24 hour inhalation of about 2500 ug/m^3, which produced about a 25% increase in incidence above controls. This would produce risk estimate not dissimilar from that estimated here.

[3]Concentrations in air over an indoor swimming pool and the high value measured by Hartwell, at al (1984b) were not included.

[4]The experiment used by Gold, et al (1984) to estimate the TD50 was classified equivocal by NTP (RTECS, 1984). 1,1-dichloroethane was only detected in 2 of 17 measurements (Wallace, et al., 1982). The concentration used is one-half the limit of detection in the study.

[5]MLE and UCL(95%) were estimated as described in Methods from overall rates of alveolar/bronchiolar neoplasms in male mice as reported by NTP, p149(1986). The EPA value was calculated from their unit risk estimate of $4.1x10^{-6}$ (EPA,1985d).

[6]MLE and UCL(95%) were estimated from experimental results used by Gold, et al to calculate the most potent TD50 (L. Gold, personal commun.). These were nasal squamous cell carcinomas in male rats that survived at least 24 months or that died naturally before 24 months. The EPA estimate was based on a unit risk value of $1.3x10^{-5}$ (EPA,1986).

[7]The experiment from which estimates were made was considered not conclusive by NTP (Gold, et al., 1984).

[8]Calculated from a unit risk estimate of $4.8x10^{-7}$ (EPA,1985e).

[9]Calculated from a unit risk estimate of $1.3x10^{-6}$ (EPA, 1985c).

[10]Calculated from a unit risk estimate of $5x10^{-5}$ (EPA, 1985b).

[11]Calculated form a unit risk estimate of $2.6x10^{-5}$ (EPA,1985f).

Table 4. Percent of exposed population at greater than 10^{-3} risk

	Concentration Distribution of Chemical (ug/m^3)[1]		Concentration for 10^{-3} Risk[2] (ug/m^3)			Percent of Population at > 10^{-3} Risk[3]		
	GM	GSD	MLE	LCL	TD50	MLE	LCL	TD50
Benzene	37	2.48	305	190	240	1.0	3.6	2.0
Formaldehyde	22.9	1.73	342	79	5.5	z=4.93	1.2	>99.0
Carbon tetrachloride	6.03	1.87	210	146	180	z=5.67	z=5.09	z=5.42
Tetrachloroethylene	16.2	2.28	580	446	120	z=4.34	z=4.02	0.75
Trichloroethylene	12.7	3.47	1170	880	630	0.014	0.03	0.08

[1]Geometric mean (GM) and geometric standard deviation (GSD) were calculated from the data of DeBortoli, et al (1985).
[2]The maximum liklihood estimate (MLE) and 95% lower confidence limit on dose (LCL) were estimated using GLOBAL82; values in the TD50 column were calculated from the TD50, assuming linearity. The unit risk factors derived by EPA were not used in this table because we did not wish to assume linearity would necessarily be a valid assumption up to the 10^{-3} risk level.
[3]To determine this fraction we used Normal Probability Error Function tables. For example, for benzene MLE estimate: (ln 305 - ln 37)/ln 2.48 = 2.32 = z. This, in the error function table, corresponds to 0.4898. Thus, the fraction of the which population distribution above 305 ug/m^3 is 0.5 - 0.4898, or about 1%. The value of z has been listed instead of percent for all z > 3.9 (percent < 0.01).

Table 5. House-by-house cancer risk based upon one study (DeBortoli, et al., 1985)

	Houses (Risk x 10^{-5})[1]															CV(%)[2]	Range (max/min)
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15		
Benzene (7.4/14)	4.8	5.8	8.5	9.0	35	33	12	10	48	56	19	43	21	16	110	97	23
Carbon tetrachloride (.95/1.4)	2.7	2.0	1.4	2.7	7.5	6.8	4.8	4.1	6.1	3.4	5.4	8.1	8.1	1.4	7.5	51	6.0
Chloroform (2.7/2.6)	<1.0	<1.0	<1.0	<1.0	1.0	16	<1.0	2.1	1.0	8.3	2.1	<1.0	<1.0	<1.0	<1.0	>160	>8.3
Dichloromethane (2.7/225)	4.7	<0.12	<0.12	<0.12	<0.12	60	4.3	3.5	2.9	<.06	36	<.06	<.06	2.7	7.1	>210	>1000
Formaldehyde (51/53)	50	19	8.7	26	48	30	39	25	14	16	24	28	25	7.7	15	51	6.5
Tetrachloro-ethylene (1.0/4.5)	7.3	1.8	2.7	2.0	0.67	4.4	2.2	2.9	7.6	1.8	6.9	5.6	14	2.2	10	78	21
Trichloro-ethylene (0.39/3.4)	1.6	.11	.92	.46	.34	1.4	.80	2.3	1.1	.80	9.9	4.8	13	2.4	3.0	130	120
Total Risk:	72	30	23	41	93	152	64	50	81	86	103	91	82	33	154	52	6.7

[1]The 95% upper confidence level risk estimated for mean indoor air concentrations, as shown in Table 3, was divided by the mean concentration to approximate a 'unit-risk' factor. This was then multiplied by the concentrations measured in each house.

[2]CV = coefficient of variation = (standard deviation of risk)/(mean risk).

[3]The numerator is the 95% upper confidence level (UCL) risk ($x10^{-5}$) estimated from mean indoor concentrations (see Table 3). The denominator is the mean concentration in all homes for which we have data.

LAWRENCE BERKELEY LABORATORY
TECHNICAL INFORMATION DEPARTMENT
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA 94720